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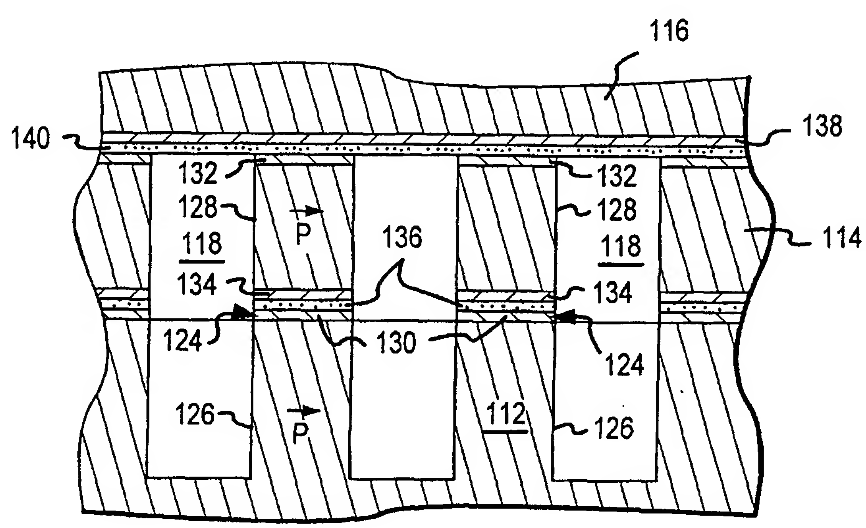

(57) Abstract

An inhaler provides a controlled delivery of an inhalant and includes an inhaler housing (1) and a mouthpiece (5) coupled to the inhaler housing (1). A piezoelectric dispenser–head (14) is coupled to the inhaler housing (1) and configured to be coupled to the dispensing chamber (10). The piezoelectric dispenser–head (14) includes an array of dispensing channels (118) and an array of dispensing nozzles (15). The array of dispensing channels (118) are formed with actuatable walls (124) made at least partially of a piezoelectric material. Application of an electric field to selected side walls reduces a volume in an associated channel and creates a pressure pulse of flowable substance in the associated channel through a dispensing nozzle.

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PIEZO INHALER

BACKGROUND OF THE INVENTION

Field of the Invention

This invention relates to an inhaler, more particularly to an inhaler with a piezoelectric dispenser-head.

Description of Related Art

There are currently three main methods for drug delivery via the respiratory tract, namely metered dose inhalers, dry powder inhalers, and nebulizers.

Metered dose inhalers ("MDI") are widely used in the management of asthma. The MDI comprises a drug packaged with a propellant in a pressurized aerosol container can having a valve which releases a volumetric metered dose of aerosol upon actuation. These inhalers are portable, small, and convenient to carry but deliver a dose which varies in quantity, delivery speed, and droplet size distribution as the vapor pressure of the propellant varies. The propellant pressure varies with temperature and decreases progressively as the content becomes depleted so that the range in dose variation may be substantial. Incomplete evaporation of the propellant may cause "sticking" and localized concentration of drug droplets at an impact area, and this in turn can cause undesirable side effects. For example bronchosteroids can cause local immuno-suppression and local fungal infection while local concentration of bronchodilator can lead to swallowing, with unwanted systemic affects. In addition, the use of an MDI requires a degree of synchronization between manual valve actuation and inhalation which many users find difficult.

Dry powder inhalers ("DPI") devices rely upon a burst of inspired air to fluidize and draw a dose of an active powder into the bronchial tract. While this avoids the synchronization problem of the MDI, DPI's are sensitive to humidity and may provoke asthma attacks in some individuals sensitive to inhaled powder. Moreover, because the force of inspiration varies from person to person, the dose administered varies.

Nebulizers generate an aerosol by atomizing a liquid in a carrier gas stream and require a continuous gas compressor or bulky supply of compressed gas. In general, the

droplet size of the aerosol is a function of carrier gas pressure and velocity and hence cannot be easily varied independently of concentration of the active substance in the gas stream. Inhalation reduces the pressure at the nebulizer nozzle and thus dosage and particle size are also influenced by the duration and strength of each breath. Most nebulizers operate continuously during inhalation and exhalation but special control systems can be employed to meter the aerosolized gas flow from the nebulizer to a holding chamber from which the user may draw a charge.

In general the precision of dose delivery of each of these devices is less accurate than desirable and restricts their use to drugs which have broad dosage tolerance. In each case delivery of the active agent to the intended application site is overly dependent on user technique and is variable from dose to dose and person to person. Not only is an improved delivery system required to optimize current nasal and pulmonary therapies utilizing locally acting drugs but there has long been recognized a potential for the administration of many additional local and systemic drugs if a more satisfactory means of delivery were available. Medical advances suggest that pulmonary delivery of drugs such as peptides, proteins and analgesics might be of considerable advantage compared with conventional oral or injection delivery means. For example it has been suggested that insulin for diabetics may be delivered via the pulmonary route if a suitable means of delivery were available. The deposition of drug particles on lung tissue is a function of size, shape and density of particles or droplets. For many drugs, control of one or more of these factors along with precise dose or dose rate control would be desirable. However, at the present time no means of drug delivery is available which adequately meets such requirements.

Many attempts have been made to provide a cigarette substitute which provides nicotine by inhalation but which avoids the need for combustion of tobacco. Provision of a cigarette substitute involves complexities additional to those involved in the administration of a therapeutic agent. Although it is relatively easy to administer nicotine (for example in tablet form, via transdermal patches and the like), such forms do not satisfy habitual smokers because they do not satisfy important complex physiological and psychological affinities acquired by habitual smokers of combustible cigarettes.

In an attempt to provide an acceptable alternative, many cigarette substitutes have been proposed which provide nicotine on inhalation without combustion of tobacco. Conceptually, such devices are less harmful to the inhaler than smoking, avoiding the hazards of passive smoking among bystanders, and the fire hazard and environmental problems associated with cigarette smoking. However, despite these major advantages, no device so far proposed has met with consumer acceptance.

Early cigarette substitutes employed a porous carrier impregnated with a liquid nicotine containing composition through which an air stream could be drawn to volatilize nicotine. This approach yielded insufficient nicotine per puff, suffered from a tendency for the carrier to dry out and delivered a variable amount of nicotine per puff, depending on factors such as air temperature, humidity, lung capacity of the user and amount of liquid composition remaining in the carrier.

Subsequent devices delivered nicotine from a pressurized aerosol container from which nicotine can be released by mechanical valve actuator. In one such device the valve is microprocessor controlled to limit the frequency and duration of actuation. However, the dose delivered varies with the vapor pressure of aerosol remaining in the container as well as with duration of valve actuation. The disposable pressure container, aerosol valve, and CFC propellant add considerably to active substance cost. These devices share the disadvantages of MDI devices previously discussed.

In yet other devices a nicotine containing substance is heated to vaporize an amount of nicotine which is then available for inhalation. The amount of nicotine delivered by such devices is difficult to control and is temperature dependant. In one such device a plurality of nicotine-containing pellets may be heated sequentially so that each liberates a predetermined dose. However, in that case, the dose is fixed during pellet manufacture, particle size of the aerosol is uncontrolled, and temperature of the inhaled air cannot be varied independently of dose.

Factors such as the quantity of nicotine per puff, the temperature of the puff, the draw, the presence and size distribution of flavor particles in the puff and like factors are of considerable importance in satisfying habitual smokers. The various alternatives proposed to date have simply proved unacceptable to most smokers.

To date no device has provided a satisfactory means of adjusting both the quantity of nicotine delivered in each puff in response to user demand and/or maintaining adequate precision and accuracy in the dose quantum metered out. Further the devices have failed adequately to mimic the sensations obtained during smoking.

SUMMARY OF THE INVENTION

An object of the invention is to provide an inhaler.

Another object of the invention is to provide an inhaler that delivers a variety of different medicaments.

Yet another object of the invention is to provide an inhaler that provides controlled delivery of a medicament.

Still another object of the invention is to provide an inhaler that can be substituted for a cigarette.

A further object of the invention is to provide an inhaler that includes a piezoelectric dispenser-head.

A further object of the invention is to provide an inhaler that includes a piezoelectric dispenser-head and an array of dispensing channels.

These and other objects of the invention achieve an inhaler that dispenses a flowable substance. The inhaler includes an inhaler housing and a mouthpiece coupled to the inhaler housing. A piezoelectric dispenser-head is coupled to the inhaler housing and configured to be coupled to the dispensing chamber. The piezoelectric dispenser-head includes an array of channels and an array of dispensing nozzles. The array of channels are formed with actuatable walls made at least partially of a piezoelectric material. Application of an electric field to selected side walls reduces a volume in an associated channel and creates a pressure pulse of flowable substance in the associated channel through a dispensing nozzle.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 is a schematic part sectional perspective view of one embodiment of an inhaler (cigarette substitute) according to the invention;

Figure 2(a) is a schematic section in an axial plane of the inhaler of Figure 1;

Figure 2(b) illustrates in a schematic section another embodiment of the inhaler of Figure 1 that includes a dispensing head with first and second sides, first and second dispensing channels, each of which is coupled to a dispensing nozzle;

Figures 3A, 3B and 3C are graphs showing the dispensation of an active ingredient (hatched) as a function of inhalation time in use of the embodiment of Figure 1;

Figure 4 is a schematic perspective view of a second embodiment of the invention;

Figure 5 is a schematic diagram of a third embodiment of the invention;

Figure 6 is a perspective view of a schematically illustrated piezoelectric dispenser-head; and

Figure 7 is an enlarged partial cross-sectional view of the dispenser-head of Figure 6 taken along line 7-7 illustrating a parallel channel array of the dispenser-head.

DETAILED DESCRIPTION

According to a further aspect and by way of initial summary, the invention consists in a method for administering a substance to a human or animal subject by inhalation, said method comprising the steps of:

(i) ejecting a predetermined number of discrete droplets of the substance from at least one droplet ejection device in response to actuation signal, and

(ii) entraining the droplets in an inhalation airstream.

According to another aspect, the invention consists in a method for topical application of a substance to a human or animal subject comprising the steps of:

(1) ejecting a predetermined number of discrete droplets of the substance from at least one droplet ejection device in response to an actuation signal, and

(2) directing the droplets at a selected area or region of the subject.

According to yet another aspect, the invention consists in an apparatus for administering a substance to human or animal subject, said apparatus comprising:

a droplet ejection device containing a substance to be administered, means responsive to an actuation signal to eject a predetermined number of discrete droplets of the substance, and

means for directing the ejected droplets at, or into, the subject.

The substance to be administered may be a therapeutic or other physiologically active agent and may be a liquid, a solution or a suspension for example a colloidal solid in a liquid carrier or an emulsion. In one aspect of the invention, the droplet ejection device ("DED") may be a piezoelectric device generally of the kind used in ink jet printing or is a thermal "bubble jet" of the kind used in ink jet printing.

These devices are sometimes referred to as "droplet on demand" devices. By way of example, piezoelectric devices are broadly described in "Ink-Jet Printing" [M. Doring Phillups Tech Rev 40, 192-198, 1982 No. 7], while thermal jet devices are broadly described in "Thermal Ink – Jet Print Cartridge Designers Guide" (2^{nd} Edition Hewlett Packard), both incorporated herein by reference.

Briefly, a typical thermal device consists of a liquid-containing chamber provided with an array of twelve coaxially divided nozzles and has twelve thin film resistors, a resistor being located directly behind each nozzle. Each nozzle supplies a droplet of liquid from the chamber if and when the corresponding resistor is energized by a short electrical pulse. The resistors thus function as ejection means. Within a few microseconds liquid in contact with resistor is vaporized and forms a bubble. The vapor bubble grows rapidly and imparts momentum to liquid above the bubble. Some of this liquid is ejected as a droplet from the adjacent nozzle at a velocity typically exceeding 10 meters/second. The ejected volume of liquid is automatically replaced in the chamber from a reservoir by capillary action or by atmospheric pressure acting on collapsible reservoir bladder, a piston or the like. Devices of this kind when used for printing eject a typical drop of about 50 micron diameter at velocities in excess of 10 meters/second and are capable of drop ejection frequencies of up to several thousand droplets per second. The piezoelectric device generates a droplet by means of a pressure wave in the fluid produced by applying a voltage pulse to a piezoelectric ceramic which in this device acts as the ejection means. As with the thermal device, the droplet is ejected through a fine aperture. The fluid is ejected in the form of a fine droplet whose velocity depends

on the energy contained in the voltage pulse. In conventional ink jet applications, ejection velocities in excess of 2 meters/second with droplet diameters around 150 microns and droplet ejection rates in excess of 6,000 droplets per second can be achieved.

Although conventional "droplet on demand" or "droplet ejection" devices such as used in ink jet printers may be employed in embodiments of the invention, the droplet ejection devices for use in the invention preferably differ from those used for printing. With print heads the ejection orifices are typically arranged as a rectangular matrix of, for example, 2 x 6 or 4 x 6 orifices, the droplets being expelled in parallel direction from various combinations of orifice, to form characters on a paper moving past the print head at a distance of from 0.7 mm to 1.0 mm from the orifice. Droplet size is chosen to provide optimum print quality and high dot resolution. For use in the present invention there may be a smaller or greater number of orifices than used for printing and there is no need for the orifices to be arranged in a rectangular matrix with parallel orifice axes. The droplet ejection orifices may, for example, be arranged in a circle and/or maybe directed at a converging or diverging angle to the axis of each other. Also for use in the present invention it is often preferred to eject much smaller droplets than are useful for printing. Additionally, the droplet ejection orifices may differ in diameter one from another so that the particle size of the active agent sprayed from the device may be controlled programmatically by selecting which orifices are used for droplet ejection and particle size may be varied from one time interval to another. Because the size of droplet ejected from the device in response to a predetermined signal is predetermined for a given liquid and device, and because the number and frequency of droplets ejected can be controlled with great precision, it is possible to closely control the total volume of liquid (dose) delivered in a given time interval. For example the device might deliver 1,000 droplets of 50 micron diameter in a second. This volume can in principle be increased or decreased in increments of one droplet.

In one preferred embodiment of a device according to the invention, the DED is provided with orifices of an aperture size selected to eject a droplet of less than 10 microns diameter and, more preferably, of from 1 to 5 microns diameter. Droplets may be emitted from the DED from a selected orifice in succession or from a plurality of orifices simultaneously.

In preferred embodiments the droplet delivery device or devices may be manually actuated or may actuate in response to an inhalation detector signal or other signal. The apparatus is provided with control means to eject a predetermined number of droplets. The number may be varied in response to stored data and/or other input signals and program logic may control such factors as the number of droplets ejected in a predetermined time interval, frequency of droplet ejection, the total number of droplets of active substance issued with a time period, or the like. The control means may be programmed to provide many other desirable functions as hereinafter described.

The means for directing the ejected droplets at or into the subject may for example be a simple mouthpiece provided with an air inlet, a nasal shroud, face mask or other spray directing means. The activation is typically in solution and is emitted from the DED as a fine spray which may be combined with air and/or may be heated prior to inhalation.

With reference to Figures 1, 2(a) and 2(b) there is shown a first embodiment of the invention consisting of a dispenser (hereafter referred to as an "inhaler") that can include a cigarette-shaped hollow tubular body 1 with connected body parts 2, 3. Body part 2 has a side wall 4, a mouthpiece 5 at or adjacent one end and a threaded other end 6. A plurality of axially extending slots 7 penetrate side wall 4. Body part 3 is screw threaded at one end for connection with threaded end 6 of body part 2. Body part 3 is closed or constricted at the end 9 remote from mouthpiece 5.

Nicotine in a suitable solvent (for example water) or other flowable substance is provided in a container 10 which is adapted by means of a spigot shaped outlet and coupling 11, for fluid connection to an inlet port 12 of dispenser-head 14. The dispenser-head 14 draws flowable substance from the inlet port 12 and moves it to the droplet dispensing nozzles 15. In one embodiment, dispenser-head 14 is a piezoelectric dispenser-head 14 with one or more droplet dispensing nozzles 15. In another embodiment, dispenser-head 14 includes first and second sides 14' and 14" each with a respective dispensing channel that are coupled to dispensing nozzle 15 Figure 2(b). Dispenser-head 14 is controlled by a controller 16. Suitable controllers include but are not limited to electronic and microelectronic circuits and sensors, and the like. In one embodiment dispenser-head 14 and controller 16 as well as other electrically-powered

parts are energized by means of a hollow cylindrical battery 17 via an on/off switch 18 extending through side wall 4 and operable by the user. When a user inhales at mouthpiece 5, a stream of air "A" is drawn into body 1 via slots 7, through body part 2, and mouthpiece 5 into the user's lungs. Slots 7 may be provided with a damper or the like (not illustrated) to control airflow or the device may be provided with a porous plug to control airflow ("draw") on inhalation at mouthpiece 5. A sensor 19 detects a change in pressure or airflow in the device due to inhalation or suction at mouthpiece 5 and issues an actuation signal via cables (not illustrated) to controller 16. Controller 16 responds to the actuation signal by issuing an output signal or signals via cables (not illustrated) to dispenser-head 14 according to pre-programmed parameters or algorithms as hereinafter described. The output or "dose" signal is, or includes, a set of "eject" signals for example a train of voltage pulses. Dispenser-head 14 responds to the output signal or signals by issuing a plurality of droplets of flowable substance from dispensing nozzles 15 of dispenser-head 14. The flowable substance issues from dispenser-head 14 as a fine spray of droplets which are entrained in the inhalation airflow from slots 7 towards mouthpiece 5. The spray typically comprises fine droplets which tend to vaporize in the airflow. Optionally, heating means 20 are provided. In that case the combination of air with droplets may be brought into thermally conductive contact with heating means 20 prior to leaving mouthpiece 5. This not only produces a sensation on inhalation similar to that obtained by smoking a combustible cigarette, but also serves to enhance the vaporization of active substance droplets in the gas stream reducing droplet size.

In the embodiment illustrated in Figures 1 and 2, the flowable substance container 10 is a collapsible bladder which is housed within a protective hollow cylindrical cartridge 21 having an air vent 22. However other forms of container (for example a cylinder fitted with a piston) could be used. Cartridge 21 is optional and serves to shield container 10. Container 10 is disposable or replaceable and may be adapted for fluid communication with inlet port 12 of dispenser-head 14 by means of a threaded, bayonet, or other suitably sealing connection.

Optionally, battery 17 may be of annular form and adapted to sleeve cartridge 21 to save space. The battery 17 is designed to provide sufficient electrical energy to operate

the inhaler. When inhaler is not in use there is a saving of energy. Heating means 20 may be infrared heating plates or elements, resistance elements or the like.

Controller 16 desirably comprises a programmable logic circuit for example a microprocessor together with associated electronic memory, clocks, power supply, sensors and the like and is programmed to control the quantity of flowable substance delivered by the inhaler upon inhalation, subject to predetermined criteria.

In normal operation of the inhaler a drop of pressure, or an increase in airflow, at mouthpiece 5 is detected by sensor 19 which issues a signal indicative of inhalation ("actuation" signal) to controller 16 (via cables not illustrated). Controller 16 responds by issuing a "dose" signal to dispenser-head 14 resulting in a spray of droplets from the inhaler.

The "dose" signal typically comprises a predetermined set of droplet "eject" signals which causes one or more dispensing nozzles 15 of dispenser-head 14 to eject a predetermined number of droplets. The dose signal may, for example, be a train of pulses (each pulse being a droplet eject signal) directed serially to one of the channels of the dispenser-head 14, or may be a sequence of pulses directed in parallel to a number of channels in the dispenser-head 14. Since the volume of a droplet issued from a selected dispensing nozzles 15 is predetermined for a given flowable substance and orifice, and the number of droplets ejected is controlled by the "dose" signal, the total volume of flowable substance ejected in response to the "actuation" signal is precisely determined.

Controller 16 controls the pulse spacing, pulse width, and pulse frequency of the "dose" signal as well as the number of pulses or droplet "eject" signals and therefore determines the time interval during which droplets enter the inhalation air stream i.e. the dose rate. The number of droplets issued and/or the droplet issue frequency may be altered by changing data stored in the memory of the controller 16. Controller 16 may also be programmed to address specific channels of the dispenser-head 14 so as to emit droplets from selected droplet dispensing nozzles 15 which may differ one from another for example in respect of diameter or orientation.

Controller 16 may also be programmed to provide a time delay between receipt of an actuation signal indicative of inhalation from pressure sensor 19 and the issuance of a “dose signal”. The time delay may be varied by changing data stored in a control

memory. By controlling the time delay between the leading edge of actuation signal and issue of the dose signal, and by controlling the frequency of droplet "eject" pulses in the dose signal, the active substance can, for example, be ejected into an inhaled airstream as a spike near the start (FIG. 3A) or start and end (FIG. 3B) of an inhalation "puff", or can be spread over the puff duration (FIG. 3C), or may be confined to the leading or trailing portion of a puff. This enables the change in concentration of nicotine during a puff of a cigarette to be more closely mimicked.

The control means can also be programmed to prevent a dose signal from issue until a predetermined "non repeat" time has elapsed after a preceding dose signal has been issued, notwithstanding receipt of an inhalation signal. This provides a minimal delay between successive doses.

The control means may also be provided with means for counting and storing the total number of dose signals issued within a predetermined time interval and if the total dose succeeds a predetermined limit (for example 30 doses in a 30 minute period) then the control circuit prevents further dose issue until a further period (e.g., 1 hr) has elapsed. This limits the maximum dose issued within an extended period.

In preferred embodiments of the invention the control means enters a minimum energy drain mode to conserve battery power if for example more than 5 minutes have elapsed since an inhalation was detected.

The apparatus of FIG. 1 may optionally be provided with means for signaling the doses remaining in the device for example by means of a plurality of LEDs 30 which progressively extinguish. Each LED may for example correspond to a dose equivalent to smoking one cigarette and the apparatus might initially store a dose corresponding to one (or several) packets of cigarettes. Other indicator means e.g., an LCD display, could be used.

In summary the control means allows programmable control factors such as:

(1) Predetermined number of droplets of nicotine issued in a single dose (dose volume).

(2) Frequency of drop issue within a dose (dose rate).

(3) Synchronization of the dose relative to commencement of inhalation.

(4) Injection of dose as a function of time from commencement of inhalation (pulse spacing and frequency).

(5) Control of maximum frequency of issue of successive doses or non repeat time (e.g., successive doses available at not less than 60 second intervals).

(6) Control of maximum number of doses available in a given period, i.e., maximum dose rate (e.g., no more than 20 doses available per hour).

(7) Programmed variation of dose from one actuation to another (e.g., successive reduction in dose to reduce drug dependence).

(8) Programmed variation from time to time (e.g., dose to decrease from day to day).

(9) Control of nozzles from which the droplets issue (and hence spray pattern).

(10) Discrimination for adequacy of inhalation (No dose unless accompanied by sufficient inhalation air).

It will be apparent from the above that the device can be programmed in other ways and to perform other functions by the addition of other sensors – for example temperature or humidity sensors.

In addition the control means may be provided with means by which control parameters may be altered or by which the device may be reprogrammed, for example by interfacing with a keyboard or external computer.

As can be appreciated, the microprocessor may be preprogrammed or may be user-programmable to control the operation of various DED nozzles, the heater, the airflow or the like in various other combinations, sequences, or as functions of time, temperature or the like.

Tubular body 1 may be made of any suitable material, e.g., plastics, ceramics, precious metals or the like. Mouthpiece 5 may be integral or may be soft-tip, for example of rubber or plastics cardboard, or paper and may be independently disposable. The battery may be replaceable or rechargeable. The dispenser as a whole may be provided as a disposable item or may be reusable. In the latter case, the product container and DED device will normally be replaceable or may be provided as a combined unit. In that case, the body portion will be separable, e.g., via a screw-threaded or bayonet coupling,

into sections to facilitate installation and removal of the product cartridge and/or battery. The product to be dispensed may be for example an aqueous solution of nicotine and may contain additional substances such as glycols, flavors or essences, for example menthol. The active substance may be in the form of a gel, melt, solution or suspension.

If desired, more than one DED 14 may be incorporated whereby to produce droplet streams of different droplet size and in this case, one stream may be fully vaporized by heating plates 20, while a second stream may be directed so that the user receives the sensation of a wet vapor in combination with a dry vapor as occurs when smoking conventional cigarettes.

Is not essential that the spray of active ingredient be combined with air prior to heating and if preferred the spray and/or the air may be separately heated and subsequently combined or the active ingredient may be pre-heated, e.g., by heating means in thermal communication with storage container 10. By selective programming of the controller and when using a supply of nicotine, the device can be adjusted to simulate "light" or "ultralight" cigarette nicotine levels or can be selectively adjustable therebetween. In other embodiments the air intake may be adjusted to vary the air to active substance ratio thus further to facilitate simulation of the sensation of smoking different kinds of cigarettes. The invention is of particular application for assisting those wishing to withdraw from cigarette smoking being programmable to progressively reduce the dose of nicotine obtainable. Devices according to the invention may either be pre-programmed, may be provided with simple means enabling the user to adjust dose within predetermined limits of safety or may be adapted to be programmed by a user, e.g., by connection via an interface to a computer.

Although use of a battery is preferred other energization means, for example photo cells, may be employed.

It will be understood that the apparatus described may be provided in a different form, for example of a mouthpiece which is flexible whereby the body may be held a different orientation from the mouthpiece. Similarly the battery need not be annular and may be of any suitable shape.

With reference to FIG. 4, there are shown another embodiment of the invention intended to dispense a bronchodilator. Parts in FIG. 4 which correspond function to parts

in FIG. 1 are identified with the same numerals. If the substance to be dispensed is heat sensitive it is preferred to use a piezoelectric DED. Disposable cartridge 10 of the embodiment of FIG. 4 contains for example, salbutamol. The embodiment of FIG 4 differs from that of FIG. 1 in that the body is of rectangular cross-section and in that of the shape and arrangement of components differs.

A further difference is that in the embodiment of Figure 4 the mouthpiece portion 5 is moveable hingedly between a storage position "A" in which it is in alignment with the body (shown in ghost outline in Figure 4) and an active position "B" in which it is inclined at an angle to the body portion.

The mouthpiece may swivel about a swivel pin and the swivel motion may itself actuate an on/off switch to energize the controller 16.

If desired the apparatus may be provided with manual actuation (e.g. a push-button switch, not illustrated) instead of a pressure-sensitive switch, to control the operation and initiate an "actuation" signal.

In cigarette substitute apparatus according to Figure 1, droplet sizes of the order of 1-20 micron diameter or more are acceptable. For pulmonary administration of drugs a small droplet size 1-5 micron diameter is preferred. For practical purposes droplets of below 10 micron diameter and more preferably of below 5 micron diameter are therefore preferred. If necessary, droplet size can be reduced after ejection from the dispenser-head by directing droplets at each other or at a suitable target designed to further fragment the droplets, or by injecting the droplets into an inhaled stream in a suitable manner. Optionally heating devices can be employed to vaporize the flowable substance and reduce droplet size.

Suitable drugs for delivery by the inhaler described include, by way of example only, analgesics, peptides and proteins. Other suitable agents include:

(i) B_2 -bronchodilators - salbutamol, terbutaline sulphate, fenoterol hydrobromide, pirbuterol, reproterol hydrochloride, rimiterol hydrobromide, salmeterol (used extensively for treatment of acute asthma attacks and in prophylactic asthma therapy).

(ii) Antimuscarinic bronchodilators - Ipratropium bromide, oxitropium bromide (used in management of chronic bronchitis).

(iii) Corticosteroids - beclomethasone dipropionate, budesonide: used in prophylactic asthma therapy.

(iv) Sodium chromoglycate, nedocromil sodium (used in prophylactic asthma therapy). Antibiotic Therapy:

(v) Pentamidine isethionate - (antibiotic for the prophylaxis and treatment of pneumonia due to Pneumocystis carinii, a common secondary infection in HIV/AIDS patients).

Local Action:

(vi) Range of proprietary 'Over the Counter' nasal decongestant sprays for common cold symptoms,

(vii) Corticosteroids - beclomethasone dipropionate, betamethasone sodium phosphate, budesonide, fluticasone propionate (used in prophylaxis and treatment of allergic rhinitis).

(viii) Sodium chromoglycate (used in prophylaxis of allergic rhinitis).

(ix) Anti-infective agents - e.g. dexamethasone, fusafungine, chlorhexadine hydrochloride (used in treatment of infection due to nasal staphylococci). Systemic Action

(x) Nasal administration of peptides related to antidiuretic hormone - desmopressin, lypressin (used in management of diabetes insipidus).

The apparatus for use in dispensing certain drugs may comprise programmed control means which issues a predetermined dose into each of a plurality of successive inhalations and in that case may be provided with a "dose complete" signal for example via LED 31 to indicate to a user when a full dose has been dispensed. The dose can be varied according to the composition being dispensed and the prescription for each user.

With reference to Figure 5, there is shown a further embodiment of the invention which is adapted to dispense an active substance such as an anaesthetic, antiseptic or a liquid medication by topical application rather than by inhalation.

In surgery or medical treatment it is sometimes necessary to apply an anaesthetic, antiseptic or other fluid over a local area by means of an aerosol sprayed from a pressurized container. However it is difficult to control the amount and location of spray

application. Moreover the use of CFC propellant as used in the aerosol is environmentally undesirable.

Parts of Figure 5 corresponding in function to parts in the embodiment of Figure 1 are identified by the same numerals.

With reference to Figure 5 there is shown a dispenser comprising a pen shaped hollow tubular body 1 assembled from hollow body parts 2, 3. Body part 2 has a nozzle opening 25 at one end while body part 3 is closed at the end remote from nozzle opening 25. Body parts 2, 3 are separable connected at 6, for example by inter-engaging thread formations. A container 10 is situated within body 1 and contains a flowable substance. Container 10 is in fluid connection with one or more dispenser-heads 14 via one or more conduits. In the present example dispenser-head 14 is a piezoelectric crystal device such as used in an ink jet print head. Dispenser-head 14 can be energized from a battery 17 via an "on/off" control switch 18 adapted for finger operation while the dispenser is hand held. For example the dispenser may be held between thumb and middle finger and may carry a push button switch 18 which is operable by the first finger. In the embodiment of Figure 5 when control switch 18 is actuated, dispenser-head 14 delivers flowable substance from container 10 through dispensing nozzles 15 as a spray of droplets directed outwardly from the dispenser via nozzle opening 25. The duration of the spray of droplets is determined by whether the control switch 18 is "on" or "off".

In a more highly preferred embodiment of the invention the volume of flowable substance sprayed as droplets per unit time can also be controlled. For example, the dispenser 1 is provided with one or more switches 26 (for example touch pad switches) which condition controller 16 (for example a microprocessor circuit) which in turn controls the amount of flowable substance being dispensed through dispensing nozzles 15 of dispenser-head 14 from which droplets are emitted and/or which controls the repetition rate of the dispenser-head 14 and thus the number of droplets delivered in a unit of time. Thus the droplet spray rate may be selectively light or heavy depending on the number of dispensing nozzles 15 emitting droplets and depending on the repetition rate of droplet emission.

If the dispenser-head 14 is provided with a plurality of dispensing nozzles 15 which are directed at preselected angles to the axis of the body, droplets of flowable

substance may be directed in the axial direction or selectively at predetermined angles to the axial direction by controller actuation of a selected dispensing nozzle 15, or a selected combination of dispensing nozzles 15. In this manner a spray pattern of droplets may be selected by means of a suitable finger control of one or a number of switches 26 forming part of the microelectronic circuit of controller 16. If all dispensing nozzles 15 are directed axially the spray pattern may be made selectively narrow or broad.

Alternatively switches 26 may be adapted to select between a number of predetermined total dose dispensations or an additional controller may be provided to select total dose. In such manner, if the dispenser contains for example a liquid local anaesthetic, a surgeon can select a preset quantity and spray pattern of local anaesthetic to be applied during surgery. The surgeon could thus select between application of a small, medium or large dose, at each actuation of a switch 26 and could preselect between a narrow, medium, or broad spray pattern.

If desired the controller 16 may be provided with means to prevent inadvertent excessive use, for example by limiting the maximum dose of dispensed flowable substance which can be applied within a pre-specified time period.

Also, if desired, the control circuit can be provided with security locking which overrides the "on/off" switch. For example the device might be provided with a programmable security code and might be incapable of issuing its contents unless and until a corresponding code is entered by an intending user.

For this purpose the device may have a plug 28, socket or electronic transmitter/receiver which permits the device to interface with an external computer. The external computer might then also record data indicative of use, doses issued, user identification, patient identification, or similar data. The external computer may also re-enter new data in one or more memories in the controller of the device for example dose values, time parameters, security codes. This data is then used in controlling response of the device to actuation by the user.

Other forms of hand control, for example touch sensitive switches or rotary switches may be employed instead of switches 26.

Controller 16 may utilize digital or analogue control and may employ a microprocessor, or discrete circuit components. In preferred embodiments the circuit

includes electronic memory, preferably of a type which is not erased due to lack of battery power. The circuit further desirably includes a display screen such as a single line LCD 27. The circuit may also employ a clock and be able to utilize and display date and time data and may have a key pad or equivalent input device or may rely for input upon communication with an external key pad. The LCD could be used to display data such as number of remaining doses or time and date of last dose.

Although the embodiment of Figure 5 has been described with reference to dispensation of a flowable substance it will be appreciated that the material to be dispensed can be in the form of a gel, colloid, powder suspension or any other form suitable for dispensation via the dispenser-head 14.

In a further embodiment of the invention (not illustrated) the dispenser-head is provided with a plurality of cartridges or chambers each adapted to contain a respective medication in flowable substance or solution form. Controller 16 may be programmed to provide an alarm (for example a beeper or flashing LED) at predetermined times or at predetermined times and dates. On next actuation of the device, it then delivers a predetermined dose of one medication or a combination or succession of medications each in a respective predetermined dose.

This embodiment is thus ideally suited for pre-programmed treatment of persons suffering from dementia or the like and for persons having to take a number of different medications each according to a schedule and who find self-administration confusing.

The device itself prompts the user to accept a dose and issues the appropriate doses of prescribed medication.

As will be apparent to those skilled in the art, features described in relation to one of the described embodiments may be combined with those of another.

Although the control signals have been described as pulses, those skilled in the art will appreciate that the signals can take a great variety of forms and may employ voltage or current signals, AC or DC signals, digital or analogue signals or the like, as required for operation of the dispenser-head selected. It is not necessary literally to count signals to eject a predetermined number of droplets and it will be understood that such expediencies as issuing "eject" signals at a predetermined frequency for a selected time interval are considered equivalent and within the scope hereof. Although the invention

has been described in terms of electronic devices, fluidic devices and non electronic means of control may be employed.

Those skilled in the art will appreciate that with many dispenser-heads a principal ejected droplet sometimes has trailing satellite droplets which are very much smaller. References herein to a predetermined number of droplets refer to the number of principal droplets ejected, but if necessary the dispenser-head can be calibrated to issue a desired dose taking account of satellite drops without departing from the inventive concept hereof. Likewise it will be understood that the control of flowable substance viscosity is important and that therefore the volume of one substance issued in response to a given set of "eject" signals will not necessarily be the same as for another substance. However those skilled in the art will have no difficulty based on the teaching hereof in programming devices according to the invention to take account of these factors.

In another embodiment of the invention, a drop-on-demand type dispenser-head is employed that utilizes the distortion of a piezoelectric material to eject flowable substance and includes an array of channels in which the individual channels of the array each have side walls formed at least, in part, of a piezoelectric material. The channels are micron sized and are arranged such that the spacing between adjacent channels is relatively small. In the operation of this type of dispenser-head, flowable substance is directed to and resides in the channels until selectively ejected therefrom. Ejection of flowable substance from selected channels is effected due to the electromechanical nature of the piezoelectric side walls of the channels. Because piezoelectric material deforms when an electric field is applied there across, the side walls of selective channels deform by applying an electric field across select ones thereof. The electric field may be so selectively applied by digital or other means. This deformation of side walls of selected channels reduces the volume of the respective channels creating a pressure pulse in the flowable substance residing in those channels. The resultant pressure pulse then causes the ejection of a droplet of flowable substance from the front end of the particular channel adjacent the side walls across which the electric field is applied. The channels provide a correct delivery volume that is difficult to achieve in a single channel. Additionally, multiple channels give access to more volume of flowable substance in a shorter period of time.

As shown in Figure 6, the dispenser-head 110 includes a main body portion 112 which is aligned, mated and bonded to an intermediate body portion 114 which, in turn, is aligned, mated and bonded to a top body portion 116.

A plurality of vertical grooves of predetermined width and depth are formed through the intermediate body portion 114 and the main body portion 112 to form a plurality of pressure chambers or channels 118 (not visible in Figure 6), thereby providing a channel array forming the dispenser-head 110. In conventional manner, channels 118 are in fluid connection to an inlet port 160 and fluid container 162.

The dispenser-head 110 further includes a front wall 120 having a plurality of dispensing nozzles 122 extending therethrough. Each dispensing nozzle 122 is in fluid connection with a corresponding one of the plurality of channels 118, thereby providing droplet dispensing nozzles for dispenser-head 110.

Figure 7 shows an enlarged partial cross-sectional view of dispenser-head 110 taken along line 7--7 of Figure 6. Dispenser-head 110 includes a plurality of parallel spaced channels 118. Each channel 118 extends vertically from top body portion 116, along intermediate body portion 114 and part of main body portion 112 and extends lengthwise through dispenser-head 110. Main body portion 112 may be constructed of inactive or active material such as unpolarized or poled piezoelectric material. Top body portion 116 may be constructed of an inactive material such as unpolarized piezoelectric material.

Separating adjacent channels 118 are sidewall actuators 124, each of which include a first sidewall section 126 and a second sidewall section 128. First sidewall section 126 may be constructed of an inactive or active material such as for an unpolarized or poled piezoelectric material. In one embodiment, first sidewall section 126 is integrally formed with body portion 112. When first sidewall section 126 is constructed of an active poled piezoelectric material, it may be formed of lead zirconate titanate (PZT), polarized in direction "P" perpendicular to channels 118. Second sidewall section 128, is formed of an active material such as lead zirconate titanate (PZT) and polarized in direction "P" perpendicular to channels 118.

Mounted to the top side of each first sidewall section 126 is a metallized conductive surface 130 which can be a strip of metal. Similarly, metallized conductive

surfaces 132 and 134, also formed of a strip of metal, are mounted to the top and bottom sides, respectively, of each second sidewall section 128. A first layer of a conductive adhesive 136 is provided to conductively attach metallized conductive surface 130, mounted to first sidewall section 126, and metallized conductive surface 134, mounted to second sidewall section 128. Conductive adhesive 136 can be an epoxy. Finally, the bottom side of top body portion 116 is provided with a metallized conductive surface 138. Metallized conductive surface 138 is mounted to metallized conductive surface 132 of second sidewall section 128 by a second layer of a conductive adhesive 140. In this manner, a series of channels 118, each channel being defined by the piezoelectric material of main body portion 112 along its bottom, the layer of conductive adhesive 140 along its top and a pair of sidewall actuators 124 is provided. Each sidewall actuator 124 is shared between adjacent channels 118.

A passivation coating may be applied to all exposed metallized conductive surfaces. In one embodiment, the metallized surfaces in dispenser-head 110 are electropolished prior to the deposition of passivation coatings. Dispenser-head 110 is placed in an acid bath and a voltage supply is attached to dispenser-head 110 in a manner to make the exposed metallized surfaces into the anode. When the voltage supply is energized, a slight amount of the metal of the metallized surfaces, such as surfaces 130 and 134, is removed or etched at the fluid interface which does not degrade the performance of dispenser-head 110. This minimizes the amount of exposed metal to be coated by the passivation coatings.

In an embodiment referring to Figure 6, front wall 120 is a porous membrane and droplets may be created by forcing a flowable substance through the pores of the porous membrane. In a further embodiment the porous membrane is positioned adjacent to the dispensing nozzles 122 of dispenser-heads 110. Membrane 120 has pores of sufficient size and in sufficient numbers such that when the flowable substance is forced against membrane 120 by the dispenser-head 110 the flowable substance is aerosolized and droplets suitable for inhalation are created. In one embodiment, membrane pores have a size in the range of about 0.25 to 2.5 microns. When the pores have this size the particles which escape through the pores to create the aerosol have a diameter in the range of 0.5 to 5 microns.

Droplets may be released with an air flow intended to keep the particles within this size range. The creation of small particles may be facilitated by the use of a vibration device such as the piezoelectric dispenser-head described in figure 6, which provides a vibration frequency in the range of about 800 to about 4000 kilohertz. Those skilled in the art will recognize that some adjustments can be made in the parameters such as the size of the pores from which fluidic medium is released, vibration frequency, pressure, and other parameters based on the density and viscosity of the formulation to be aerosolized particles having a diameter in the range of about 0.5 to 20 microns.

Membrane 120 may include pores which have a diameter in the range of about 0.25 micron to about 6 microns and a pore density in the range of 1X10 sup 4 to about 1X10 sup 8 pores per square centimeter. Membrane 120 may be made of material having a density in the range of about 0.25 to 3.0 mg/cm^2, more preferably about 1.7 mg/cm sup 2, and with a thickness of about 2 to about 20 microns, more preferably 8 to 12 microns. Alternatively, membrane 120 can be an area of pores with a diameter in the range of 0.25 micron to about 6 microns; which pores are positioned over the area of about 1 sq. mm. to about 1 sq. cm.; and which area contains from 10 to 10,000 pores.

The material of the membrane has sufficient structural integrity so that it is maintained intact (will not rupture) when the material is subjected to force sufficient to aerosolize the flowable substance. That force can be in range of 20 to about 200 psi while flowable substance is forced through the pores of membrane 14.

Membrane 120 can be made of a hydrophobic material including but not limited to polycarbonates, polyesters, and the like, with the pores being formed by anisotropic etching, etching through a thin film, and the like. The membrane material can include pores of different geometric configurations including but not limited to cylinders, non-cylinders, spherical, non-spherical, hour-glass, conical, square, rectangular and irregular shapes. When a conical configuration is used it is designed with the narrowest point of the conical configuration having an opening with a diameter in the range of 0.2 micron to 6 microns.

The foregoing description of a preferred embodiment of the invention has been presented for purposes of illustration and description. It is not intended to be exhaustive or to limit the invention to the precise forms disclosed. Obviously, many modifications and variations will be apparent to practitioners skilled in this art. It is intended that the scope of the invention be defined by the following claims and their equivalents.

CLAIMS

What Is Claimed Is:

1. An inhaler dispensing a flowable substance, comprising:

an inhaler housing;

a mouthpiece coupled to the inhaler housing; and

a piezoelectric dispenser-head coupled to the inhaler housing and configured to be coupled to a dispensing chamber, the piezoelectric dispenser-head including an array of dispensing channels and an array of dispensing nozzles, the array of dispensing channels formed with actuatable walls made at least partially of a piezoelectric material, wherein upon application of an electric field to selected side walls reduces a volume in an associated channel and creates a pressure pulse of the flowable substance in the associated channel through a dispensing nozzle.

2. The inhaler of claim 1, further comprising:

a plurality of actuators, each of an actuator being coupled to an actuatable wall.

3. The inhaler of claim 2, wherein each actuator is formed of a first section and a second section.

4. The inhaler of claim 3, wherein the second sections of the actuators are at least partially formed of a piezoelectric material.

5. The inhaler of claim 4, wherein the first sections of the actuators are at least partially formed of a piezoelectric material.

6. The inhaler of claim 4, wherein the first sections are formed of a non-piezoelectric material.

7. The inhaler of claim 1, further comprising:

a porous membrane positioned adjacent to the array of dispensing nozzles.

8. The inhaler of claim 7, wherein the membrane has sufficient porosity to emit the flowable substance as an aerosol.

9. The inhaler of claim 7, wherein the membrane has sufficient porosity to provide droplets of flowable substance with diameters of less then 10 microns.

10. The inhaler of claim 7, wherein the membrane has pores with diameters in a range of 0.25 to 6 microns.

11. The inhaler of claim 7, wherein the membrane is made of a hydrophobic material.

12. The inhaler of claim 1, wherein dispensing channels in the array of dispensing channels are parallel to each other.

13. The inhaler of claim 1, further comprising:

an actuation sensor coupled to the dispenser-head, the actuation sensor generating an actuation signal in response to a detection of an inhalation to actuate the dispenser-head.

14. The inhaler of claim 1, further comprising:

a controller coupled to the dispenser-head.

15. The inhaler of claim 14, wherein the controller includes a microprocessor.

16. The inhaler of claim 14, wherein the controller includes a microelectronic circuit.

17. The inhaler of claim 14, wherein the controller includes a microprocessor coupled to a microelectronic circuit.

18. The inhaler of claim 14, wherein the controller is a programmable logic circuit.

19. The inhaler of claim 14, wherein the controller is positioned in the inhaler housing.

20. The inhaler of claim 14, wherein the controller produces a dose signal in response to an actuation signal.

21. The inhaler of claim 20, wherein the dose signal is selected from the group of a voltage, current, AC, DC, digital and analog signal.

22. The inhaler of claim 20, wherein the dispensing chamber ejects the portion of the flowable substance from at least one of the plurality of dispensing nozzles as droplets.

23. The inhaler of claim 22, wherein the controller provides an ejection of a predetermined number of droplets in a selected dose volume.

24. The inhaler of claim 22, wherein the controller provides a frequency of droplet ejection defining a dose rate.

25. The inhaler of claim 22, wherein the controller provides a synchronization of an inhalation detection and initiation of a droplet creation.

26. The inhaler of claim 22, wherein the controller provides a time spacing and frequency of droplet ejection.

27. The inhaler of claim 22, wherein the controller provides a delivery of a controlled volume of droplet ejection during a selected period of time.

28. The inhaler of claim 22, wherein the controller provides a selection of droplet delivery from at least one of the plurality of dispensing nozzles.

29. The inhaler of claim 22, wherein the controller provides a delivery of a predetermined number of droplets.

30. The inhaler of claim 22, wherein the controller provides a controlled rate of droplet delivery.

31. The inhaler of claim 22, wherein the controller counts and stores a number of dosage signals for a predetermined length of time.

32. The inhaler of claim 31, wherein the controller generates a dose signal in response to a counting and storage of the number of dose signals for the predetermined length of time.

33. The inhaler of claim 22, wherein the controller provides a time delay between a receipt of the actuation signal and an issuance of the dose signal.

34. The inhaler of claim 22, wherein the controller provides a dose complete signal.

35. The inhaler of claim 22, wherein the dose signal is a plurality of ejection signals.

36. The inhaler of claim 14, further comprising:

an on/off switch coupled to the controller.

37. The inhaler of claim 1, wherein the mouthpiece is detachably coupled to the inhaler housing.

38. The inhaler of claim 1, further comprising:

a reservoir housing for the flowable substance detachably coupled to the inhaler housing, the reservoir housing including an embedded chip.

39. The inhaler of claim 38, further comprising:

a pin code coupled to the reservoir housing.

40. The inhaler of claim 1, wherein the inhaler produces a vaporized fluidic medium with droplet sizes of 10 microns or less.

41. The inhaler of claim 1, wherein the inhaler produces a vaporized fluidic medium with droplet sizes of 5 microns or less.

42. An inhaler dispensing a flowable substance, comprising:

an inhaler housing;

a mouthpiece coupled to the inhaler housing; and

a piezoelectric dispenser-head coupled to the inhaler housing, the dispenser-head including a first side with a first dispensing channel and a second side with a second dispensing channel, each of the first and second dispensing channels being coupled to a dispensing nozzle.

43. The inhaler of claim 42, further comprising:

a membrane positioned adjacent to each of a dispensing nozzles.

44. The inhaler of claim 43, wherein the membrane has sufficient porosity to emit the flowable substance as an aerosol.

45. The inhaler of claim 42, further comprising:

an actuation sensor coupled to the dispenser-head, the actuation sensor generating an actuation signal in response to a detection of an inhalation to actuate the dispenser-head.

46. The inhaler of claim 45, further comprising:

a controller coupled to the dispenser-head.

47. The inhaler of claim 46, wherein the controller includes a microprocessor.

48. The inhaler of claim 46, wherein the controller includes a microelectronic circuit.

49. The inhaler of claim 46, wherein the controller includes a microprocessor coupled to a microelectronic circuit.

50. The inhaler of claim 46, wherein the controller is a programmable logic circuit.

51. The inhaler of claim 46, wherein the controller is positioned in the inhaler housing.

52. The inhaler of claim 45, wherein the controller produces a dose signal in response to the actuation signal.

53. The inhaler of claim 52, wherein the dose signal is selected from the group of a voltage, current, AC, DC, digital and analog signal.

54. The inhaler of claim 52, wherein the dispenser-head ejects the portion of the flowable substance from the dispensing nozzles as droplets. .

55. The inhaler of claim 54, wherein the controller provides an ejection of a predetermined number of droplets in a selected dose volume.

56. The inhaler of claim 54, wherein the controller provides a frequency of droplet ejection defining a dose rate.

57. The inhaler of claim 54, wherein the controller provides a synchronization of an inhalation detection and initiation of a droplet creation.

58. The inhaler of claim 54, wherein the controller provides a time spacing and frequency of droplet ejection.

59. The inhaler of claim 54, wherein the controller provides a delivery of a controlled volume of droplet ejection during a selected period of time.

60. The inhaler of claim 54, wherein the controller provides a selection of droplet delivery from at least one of the dispensing nozzles.

61. The inhaler of claim 54, wherein the controller provides a delivery of a predetermined number of droplets.

62. The inhaler of claim 54, wherein the controller provides a controlled rate of droplet delivery.

63. The inhaler of claim 54, wherein the controller counts and stores a number of dose signals for a predetermined length of time.

64. The inhaler of claim 63, wherein the controller generates a dose signal in response to a counting and storage of the number of dosage signals for the predetermined length of time.

65. The inhaler of claim 54, wherein the controller provides a time delay between a receipt of the actuation signal and an issuance of the dose signal.

66. The inhaler of claim 54, wherein the controller provides a dose complete signal.

67. The inhaler of claim 54, wherein the dose signal is a plurality of ejection signals.

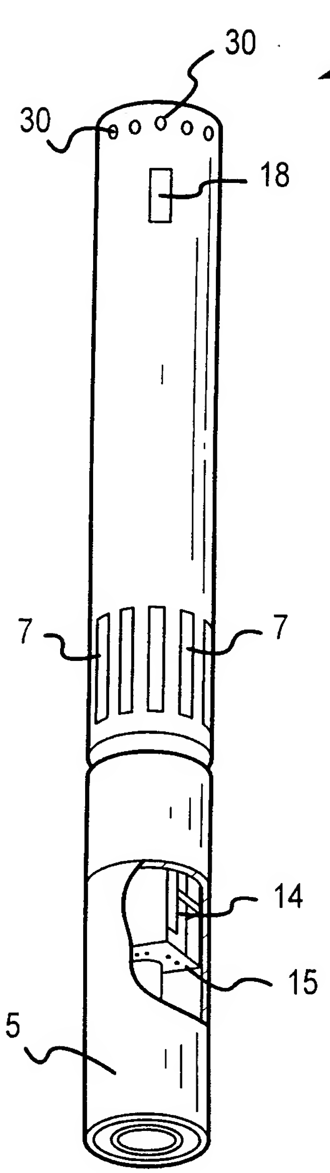
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FIG.1

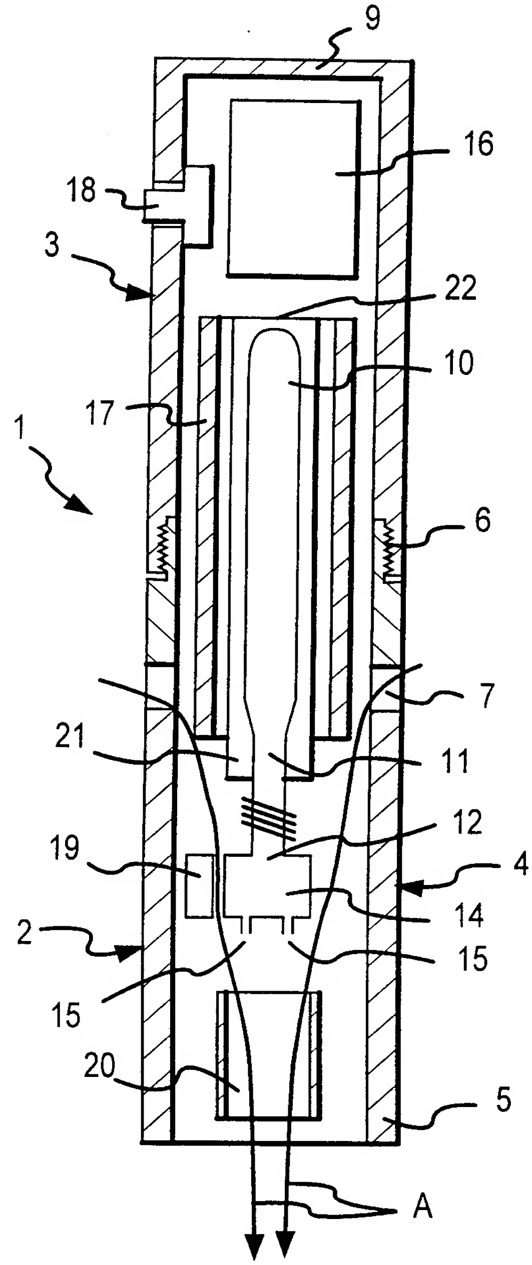
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FIG.2(a)

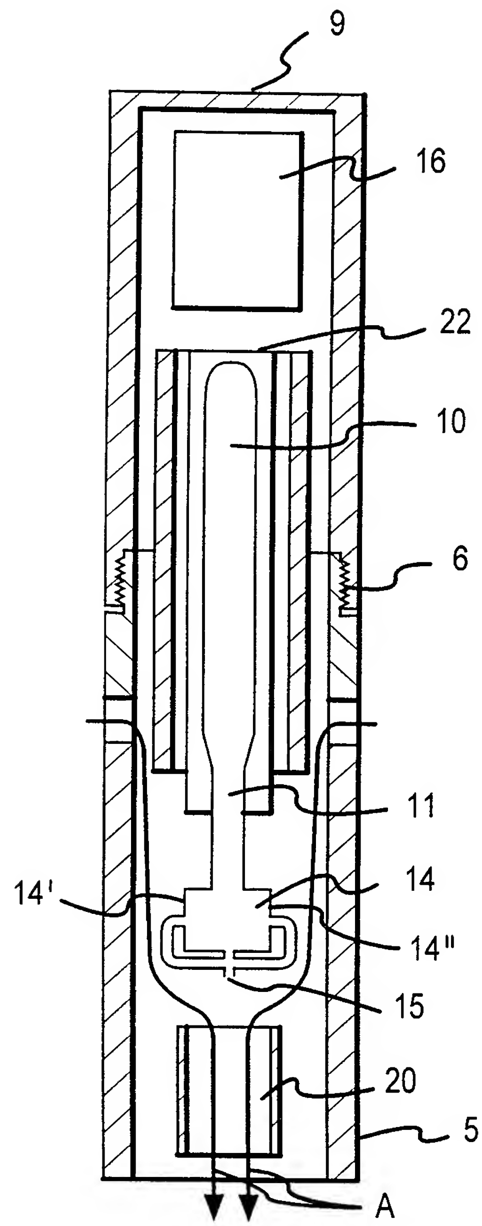

FIG.2(b)

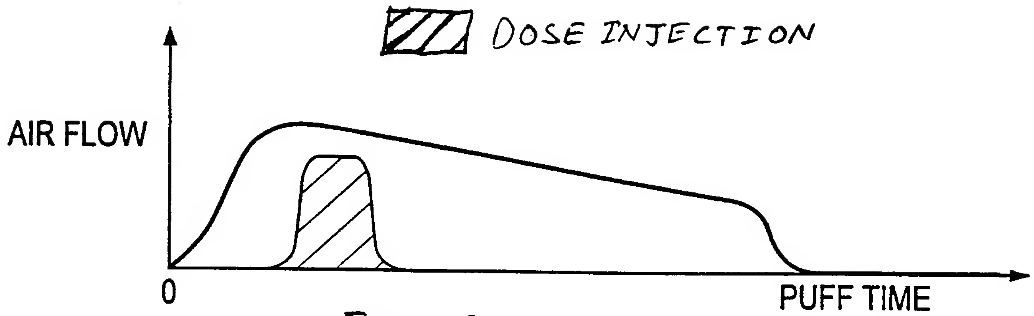

FIG. 3A

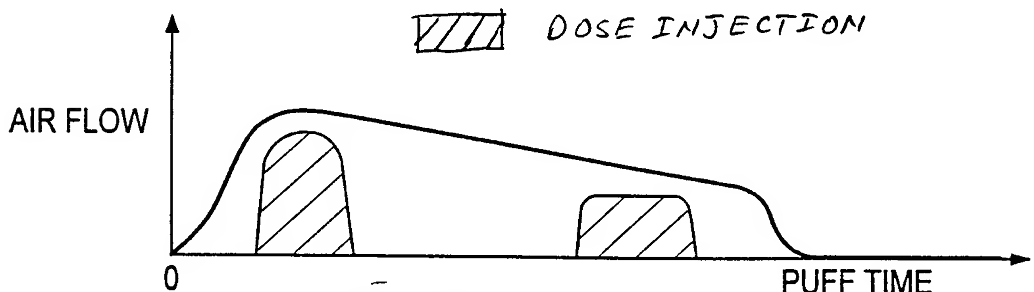

FIG. 3B

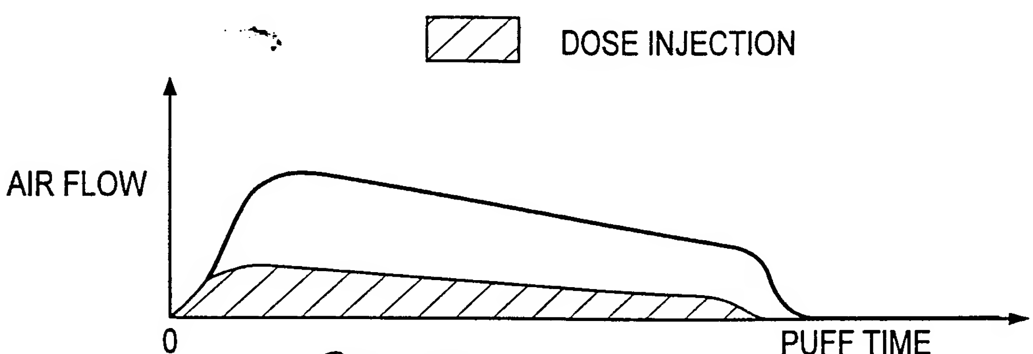

FIG. 3C

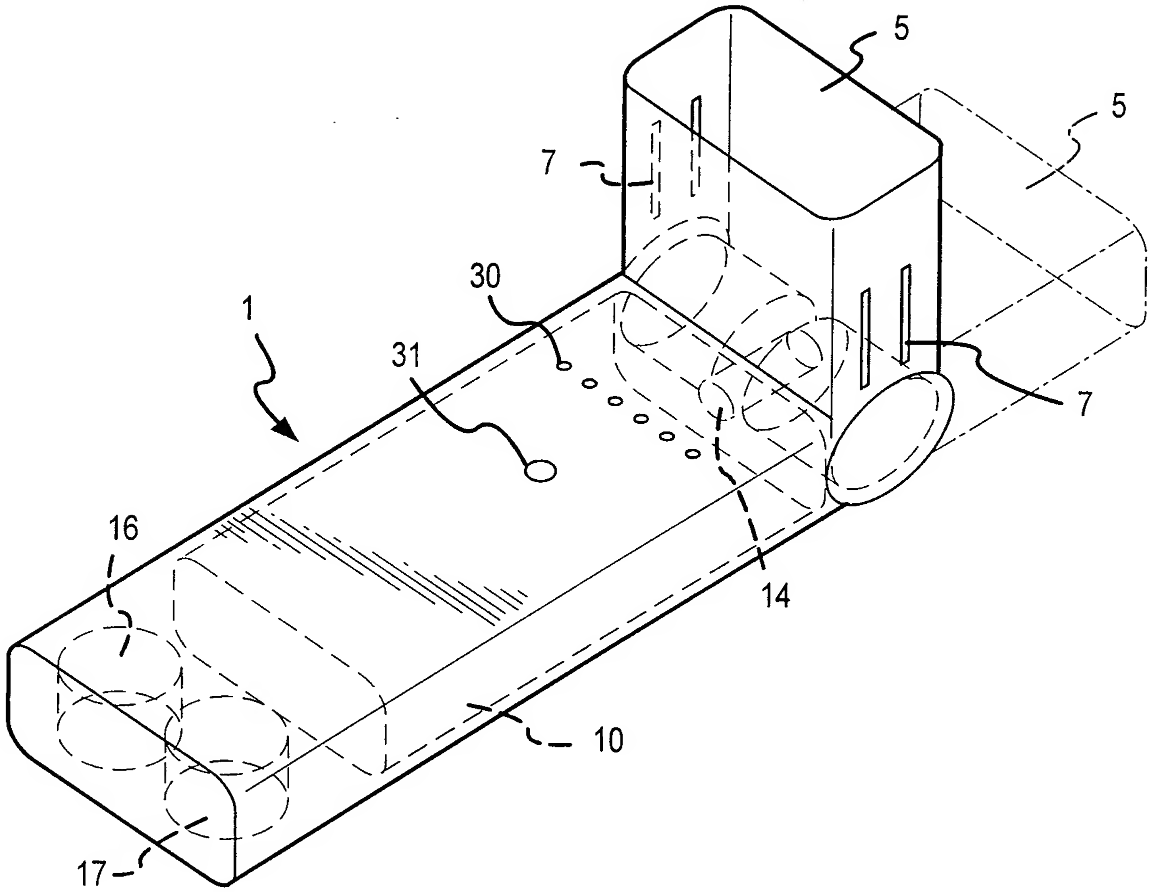

FIG.4

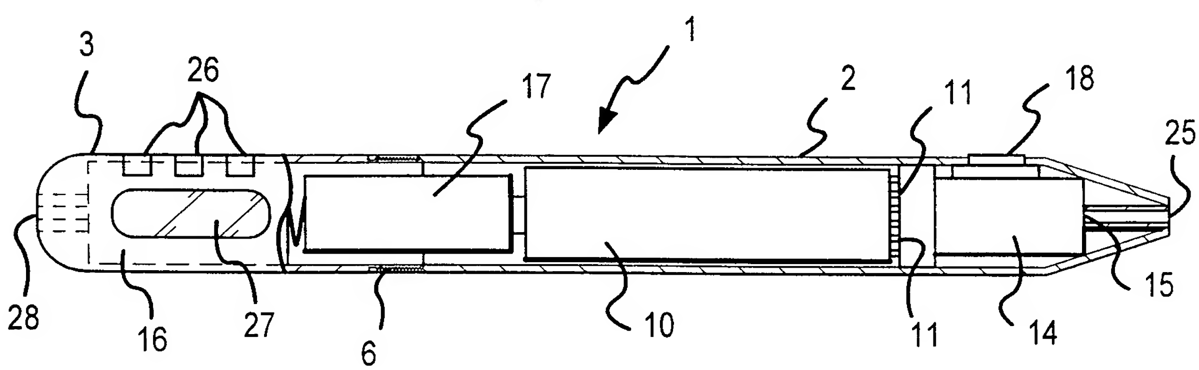

FIG.5

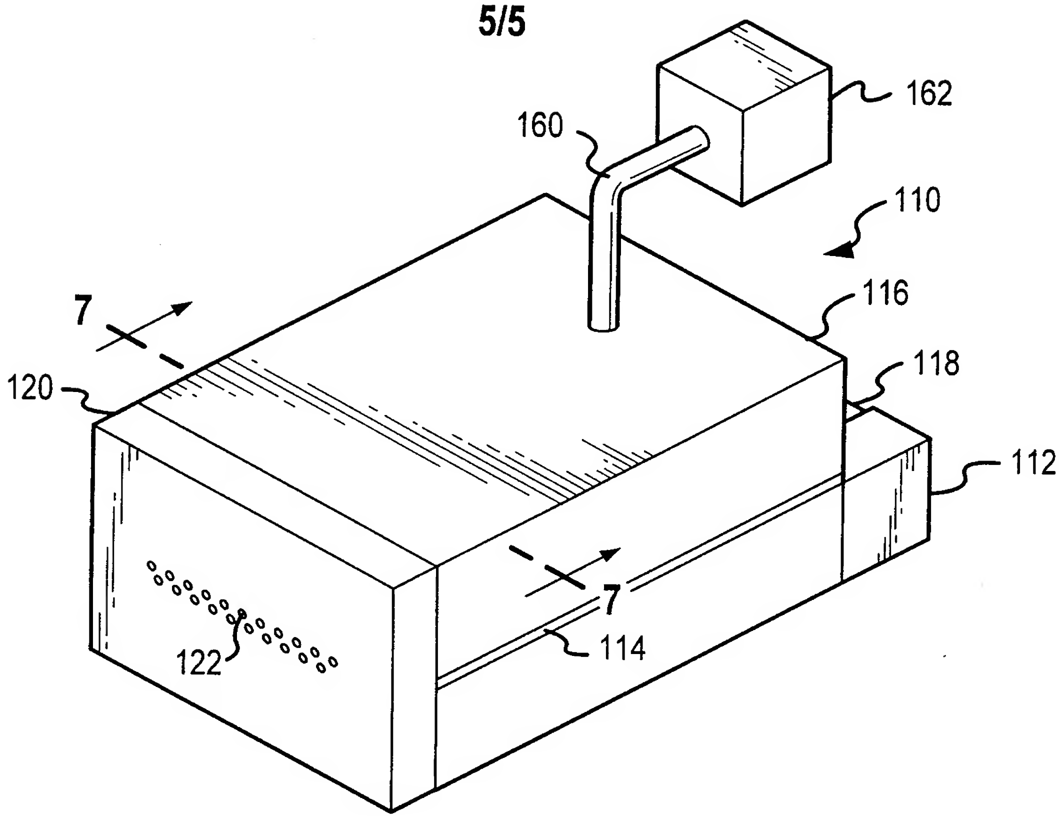
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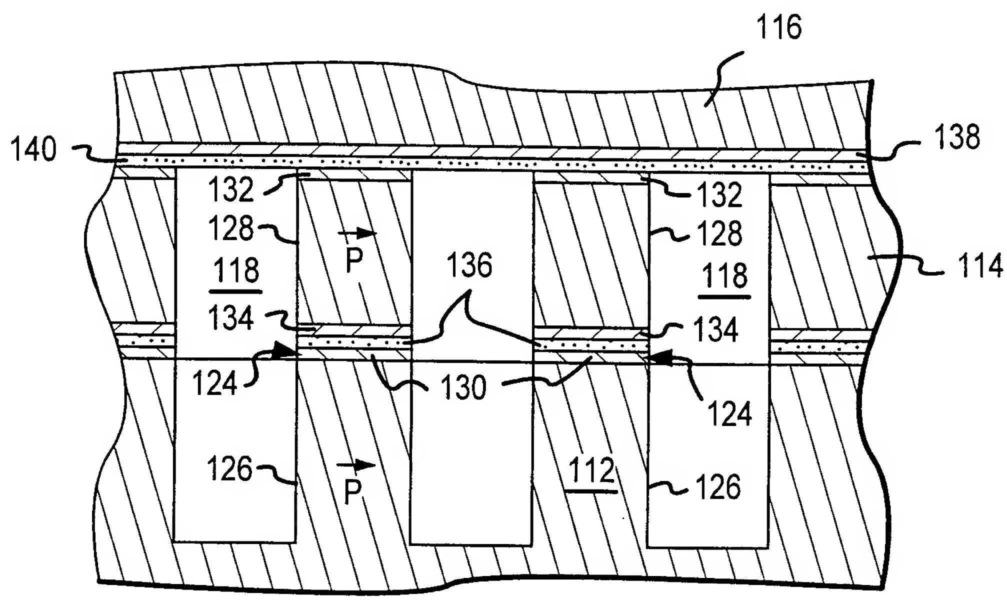
FIG.6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P

FIG.7

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/04880

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :Please See Extra Sheet.
US CL :Please See Extra Sheet.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 128/202.21, 200.12, 200.14, 200.23, 203.12, 203.15; 131/194, 327, 328; 239/4, 102.2, 406

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 5,261,601 A (ROSS et al.) 16 November 1993, Figs. 1 and 2-10; col. 2, lines 32-38; Col. 3, lines 35-43; col. 4; col. 7, lines 10-38 and col. 8, lines 10-23.	1-67 39
Y	US 5,743,252 A (RUBSAMEN et al.) 28 April 1998, Figs. 4 and 9, #41B and col. 14, lines 30-63.	39

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 MAY 2000	13 JUN 2000

Name and mailing address of the ISA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	TEENA MITCHELL
Facsimile No. (703) 305-3230	Telephone No. (703) 308-4016

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/04880

A. CLASSIFICATION OF SUBJECT MATTER:
IPC (7):

A61M 11/00, 15/00, 15/06; A24F 1/22, 11/00, 13/00; B05B 1/08, 7/10; F02D 1/06

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

128/202.21, 200.12, 200.14, 200.23, 203.12, 203.15; 131/194, 327, 328; 239/4, 102.2, 406